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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/280,567	03/30/99	BUMOL T	0409020136

HM22/0620

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EXAMINER	
BRANNOCK, M	
ART UNIT	**PAPER NUMBER**
1646	17

DATE MAILED: 06/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applic[illegible]s)
09/280,567	Bumol, TF et al
Examiner	**Group Art Unit**
Michael Brannock, Ph.D.	1646

☒ Responsive to communication(s) filed on *Jun 1, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-35* is/are pending in the applicat

Of the above, claim(s) *4, 5, and 7-35* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3 and 6* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-35* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of Application: Claims and Amendments:

1. Claims 1-35 are pending.

Response to Amendment

Claims 4, 5 and 7-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 14, 4/3/00.

The traversal is on the grounds that a search of Groups I-XVI would not be a serious burden on the examiner because the these groups relate to methods of treating various disease with a particular protein (mFLINT). This is not found persuasive for the following reasons:

Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) **or** distinct as claimed (see MPEP § 806.05- §806.05(I)): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search. These criteria were met in the above restriction. Further, a search

is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. Proteins having the same amino acid sequence as the instant FLINT are known in the art under a variety of different names: M68, TR4, TNFR-6β, DcR3. Thus, to search all of these proteins in association with all 16 categories of disease states claimed in the instant application would require divergent searches, thus to search all 16 inventions would be burdensome. Therefore, the restriction is maintained and made final.

Sequence rule compliance:

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: The specification makes reference to specific polynucleotide and polypeptide sequences (for example: page 4 and 10); these references must contain a sequence identifier of the form: SEQ ID NO: X. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-3 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 and 6 require an mFLINT protein. As there is no art recognized definition of an mFLINT protein, nor is such a definition provided in the specification, the metes and bounds of the claim Applicant is seeking protection for cannot be determined. Although the specification puts forth that the polypeptide of Figure 4 is an example of an mFLINT protein, Applicant is reminded that examples cannot define the bounds of a claim.

Claims 1-3, but not claim 6, recites the "administration of a therapeutically amount". It is unclear what this phrase means, and is most probably due to the inadvertent omission of the word "effective" between the words "therapeutically" and "amount".

Claims 1-3 (presumably) and 6 require the administration of a therapeutically effective amount of mFLINT. However, the claims do not set forth what *particularly* the mFLINT is effective at doing. The claims do not establish a relationship between the administration of mFLINT and the treatment of any of the conditions. The claims encompass conditions wherein the mFLINT administration is not directly related to the disease and does not directly help treat the disease. The claims do not put forth a step to follow which leads back and accomplishes the goal set forth in the phrase "A method of treatment"

5. Claims 1-3 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treatment comprising the administration of a protein with the amino acid sequence depicted in Figure 4, does not reasonably provide enablement for methods of treatment comprising the administration of a protein termed "mFLINT" but which does not comprise the amino acid sequence depicted in Figure 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification puts forth a protein having an amino acid sequence of that depicted in Figure 4 is *an* example of an mFLINT protein (see page 10). One of ordinary skill in the art would consider amino acid sequence variants of that depicted in Figure 4 to also be mFLINT proteins, and the definition provided by the specification encompasses these variants - which are almost infinite in number. However, the ~~specific~~ specification has provided no guidance to one of skill in the art as to which amino acid substitution/insertions/or deletions in a protein of that depicted in Figure 4 to make such that the variant protein retains the ability to treat the recited conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

EBK 6/19/00

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any

given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2; Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure, pp. 14-16). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to generate the infinite number of variants required by the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

6. Claims 1-3 and 6 are not allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, Ph.D., can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

MB

June 19, 2000